



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



(11) EP 1 348 715 A3

(12)

# EUROPEAN PATENT APPLICATION

(88) Date of publication A3:  
19.11.2003 Bulletin 2003/47

(43) Date of publication A2:  
01.10.2003 Bulletin 2003/40

(21) Application number: 03015037.9

(22) Date of filing: 21.04.1999

(51) Int Cl.7: C12N 5/10, C12N 15/62,  
C12N 15/85, C07K 16/46,  
C07K 19/00, A61K 39/395,  
A61K 48/00, G01N 33/577  
// C07K16/28

(84) Designated Contracting States:  
AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC  
NL PT SE  
Designated Extension States:  
LT LV

(30) Priority: 21.04.1998 EP 98107269

(62) Document number(s) of the earlier application(s) in  
accordance with Art. 76 EPC:  
99924816.4 / 1 071 752

(71) Applicant: Micromet AG  
81477 München (DE)

(72) Inventor: The designation of the inventor has not  
yet been filed

(74) Representative: VOSSIUS & PARTNER  
Siebertstrasse 4  
81675 München (DE)

(54) CD19xCD3 specific polypeptides and uses thereof

(57) Described are novel single-chain multifunctional polypeptides comprising at least two binding sites specific for the CD19 and CD3 antigen, respectively. Further provided are polypeptides, wherein the above-described polypeptide comprises at least one further domain, preferably of pre-determined function. Furthermore, polynucleotides encoding said polypeptides as well as to vectors comprising said polynucleotides and host cells transformed therewith and their use in the production of said polypeptides are described. In addition,

compositions, preferably pharmaceutical and diagnostic compositions are provided comprising any of the afore-described polypeptides, polynucleotides or vectors. Described is also the use of the afore-mentioned polypeptides, polynucleotides and vectors for the preparation of pharmaceutical compositions for immunotherapy, preferably against B-cell malignancies such as non-Hodgkin lymphoma.



European Patent  
Office

## PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention EP 03 01 5037  
shall be considered, for the purposes of subsequent  
proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	DE JONGE JAN ET AL.: "Bispecific antibody treatment of murine B cell lymphoma" CANCER IMMUNOLOGY IMMUNOTHERAPY, vol. 45, no. 3/4, 1997, pages 162-165, XP002076120 * abstract * * page 162, right-hand column, line 20-24 * * page 163, left-hand column, line 14-31 * * page 164, right-hand column, line 16-36 * * table 3 *	1-10, 13, 17-25, 27, 30-32	C12N5/10 C12N15/62 C12N15/85 C07K16/46 C07K19/00 A61K39/395 A61K48/00 G01N33/577 //C07K16/28
X	DE 195 31 348 A (GSF FORSCHUNGSZENTRUM UMWELT) 27 February 1997 (1997-02-27) * figure 4 * * page 4, line 30-32 * * page 4, line 61 - page 5, line 12 * * page 5, line 41-43 * * claims *	1-8, 13-16	
----- -/-			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			C07K
<b>INCOMPLETE SEARCH</b>			
<p>The Search Division considers that the present application, or one or more of its claims, does/does not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely:</p> <p>Claims searched incompletely:</p> <p>Claims not searched:</p> <p>Reason for the limitation of the search:</p> <p>Although claims 30-32 are directed to a method of treatment on the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.</p>			
Place of search		Date of completion of the search	Examiner
THE HAGUE		30 September 2003	COVONE-VAN HEES, M
<b>CATEGORY OF CITED DOCUMENTS</b> X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons &: member of the same patent family, corresponding document			

EP/C/EPC/ISA/ISA (2003/09/03)



European Patent  
Office

## PARTIAL EUROPEAN SEARCH REPORT

Application Number

EP 03 01 5037

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (INCL. I7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A,D	KUFER P. ET AL.: "Construction and biological activity of a recombinant bispecific single-chain antibody designed for therapy of minimal residual colorectal cancer" CANCER IMMUNOLOGY IMMUNOTHERAPY, vol. 45, no. 3/4, 1997, pages 193-197, XP002076121 * figure 1 * * abstract *	1-32	
A	WO 91 09968 A (CELLTECH LTD) 11 July 1991 (1991-07-11) * figures 28-6 * * page 13, line 20-23 *	11, 12	
A	WO 96 36360 A (UNIV MINNESOTA) 21 November 1996 (1996-11-21) * seq. ID n 26 * * page 13, line 11-15 *	11, 12	TECHNICAL FIELDS SEARCHED (int. CL. 7)
A	BOHLEN H. ET AL.: "Treatment of EB-virus induce B-cell LCL in SCID-HU mice using CD3xCD19 bispecific and CD28 antibodies" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, vol. 35, March 1994 (1994-03), page 510 XP002076122 a3041 * abstract *	1-13, 20, 21, 23, 24, 30-32	
A	EP 0 505 908 A (HOFFMANN LA ROCHE) 30 September 1992 (1992-09-30) * page 3, line 8-23 * * page 8, line 1-8 *	26	

-/-



European Patent  
Office

## PARTIAL EUROPEAN SEARCH REPORT

Application Number  
EP 03 01 5037

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	WO 95 11922 A (AFFYMAX TECH NV ;DOWER WILLIAM J (US); MATTHEAKIS LARRY C (US)) 4 May 1995 (1995-05-04) * page 1, line 9-15 * * page 13, line 1-20 *	29	
P,X	SCHROEDER, ANJA (1) ET AL: "A recombinant bispecific single chain antibody CD19XCD3 induces rapid B cell lymphoma-directed cytotoxicity of unstimulated human T cells." BLOOD, (NOV. 15, 1998) VOL. 92, NO. 10 SUPPL. 1 PART 1-2, PP. 511A. MEETING INFO.: 40TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY MIAMI BEACH, FLORIDA, USA DECEMBER 4-8, 1998 THE AMERICAN SOCIETY OF HEMATOLOGY., XP002115457 * the whole document *	1-28, 30-32	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
P,X	KIPRIYANOV S M ET AL: "Bispecific CD3 x CD19 diabody for T cell-mediated lysis of malignant human B cells." INTERNATIONAL JOURNAL OF CANCER, (1998 AUG 31) 77 (5) 763-72., XP002115487 * figure 1 * * abstract * * page 765, right-hand column, paragraph 2 * * page 766, right-hand column, paragraph 1 *	1-28, 30-32	

EPN FORM 100 (03.98) (FINC10)

ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.

EP 03 01 5037

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

30-09-2003

Patent document cited in search report			Publication date	Patent family member(s)	Publication date
DE 19531348	A	27-02-1997	DE	19531348 A1	27-02-1997
			WO	9708205 A1	06-03-1997
WO 9109968	A	11-07-1991	AT	129017 T	15-10-1995
			AT	124459 T	15-07-1995
			AT	159299 T	15-11-1997
			AT	208794 T	15-11-2001
			AU	664801 B2	30-11-1995
			AU	6461294 A	22-12-1994
			AU	646009 B2	03-02-1994
			AU	6974091 A	24-07-1991
			AU	649645 B2	02-06-1994
			AU	7033091 A	24-07-1991
			AU	631481 B2	26-11-1992
			AU	7048691 A	24-07-1991
			BG	60462 B1	28-04-1995
			BR	9007197 A	28-01-1992
			CA	2037607 A1	07-09-1992
			CA	2046904 A1	22-06-1991
			CA	2050479 A1	22-06-1991
			DE	69020544 D1	03-08-1995
			DE	69020544 T2	18-01-1996
			DE	69022982 D1	16-11-1995
			DE	69022982 T2	28-03-1996
			DE	69031591 D1	20-11-1997
			DE	69031591 T2	12-03-1998
			DE	69033857 D1	20-12-2001
			DE	69033857 T2	12-09-2002
			DK	460167 T3	20-11-1995
			DK	460171 T3	28-08-1995
			DK	460178 T3	22-12-1997
			DK	626390 T3	11-03-2002
			EP	0460167 A1	11-12-1991
			EP	0460171 A1	11-12-1991
			EP	0460178 A1	11-12-1991
			EP	0620276 A1	19-10-1994
			EP	0626390 A1	30-11-1994
			ES	2079638 T3	16-01-1996
			ES	2074701 T3	16-09-1995
			ES	2112270 T3	01-04-1998
			ES	2165864 T3	01-04-2002
			FI	108777 B1	28-03-2002
			FI	108776 B1	28-03-2002
			FI	108917 B1	30-04-2002
			FI	990875 A	19-04-1999
			WO	9109966 A1	11-07-1991

EP 03 01 5037

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 03 01 5037

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on the European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

30-09-2003

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9109968	A		WO 9109967 A1	11-07-1991
			WO 9109968 A1	11-07-1991
			GB 2246781 A , B	12-02-1992
			GB 2246570 A , B	05-02-1992
			GB 2268744 A , B	19-01-1994
			GB 2268745 A , B	19-01-1994
			GR 3017734 T3	31-01-1996
WO 9636360	A	21-11-1996	CA 2218898 A1	21-11-1996
			EP 0835134 A1	15-04-1998
			JP 11505704 T	25-05-1999
			WO 9636360 A1	21-11-1996
EP 0505908	A	30-09-1992	AU 664985 B2	14-12-1995
			AU 1314492 A	05-08-1993
			CA 2063035 A1	28-09-1992
			EP 0505908 A1	30-09-1992
			IE 920970 A1	07-10-1992
			JP 2562541 B2	11-12-1996
			JP 5219960 A	31-08-1993
			NZ 242056 A	27-04-1994
			ZA 9202067 A	25-11-1992
WO 9511922	A	04-05-1995	AU 8124694 A	22-05-1995
			WO 9511922 A1	04-05-1995
			US 5922545 A	13-07-1999

EPO FORM 1044B

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82